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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF PREVENTION,
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

DATE: **19 January 2010**

SUBJECT: **Thifensulfuron Methyl. Petition to Establish a Permanent Tolerance (Associated with Regional Section 3 Registration) for Residues Resulting from Food/Feed Use of the Herbicide on Safflower. Summary of Analytical Chemistry and Residue Data.**

PC Code: 128845
Decision Number: 405073
Petition Number: 9F7523
Risk Assessment Type: NA
TXR Number: NA
MRID Number: 47641801
Chemical Class: Triazinylsulfonylurea Herbicide

DP Barcode: D361945
Registration Number: 352-633
Regulatory Action: Amended Section 3
Case Number: NA
CAS Number: 79277-27-3
40CFR: §180.439
Trade Name: DuPont™ Harmony® SG

FROM: William T. Drew, Chemist
Risk Assessment Branch 2 (RAB2)
Health Effects Division (HED), 7509P

THRU: Dennis McNeilly, Chemist
RAB2/HED, 7509P

TO: Barbara Madden, RM Team 5
Risk Integration, Minor Use and Emergency Response Branch (RIMUERB)
Registration Division (RD), 7505P

This residue chemistry summary document was originally prepared under contract by Dynamac Corporation (1901 Research Boulevard, Suite 220; Rockville, MD 20850). It has been reviewed by the Health Effects Division (HED), and revised to reflect current Office of Pesticide Programs (OPP) policies.

Rec'd in PR 2/4/2

Executive Summary

Thifensulfuron methyl is a sulfonylurea herbicide (Group 2) registered to E.I. DuPont de Nemours for the control of broadleaf weeds on cereal grains (barley, field corn, oat, rice, sorghum, triticale and wheat), canola, cotton, flax and soybeans. The current registered use patterns on these crops include post-emergence, and pre-plant or at-planting burndown. Thifensulfuron methyl is absorbed through the foliage of treated weeds, inhibiting growth, causing necrosis of the growing plant, and eventual plant death.

The Interregional Research Project Number 4 (IR-4), has submitted a tolerance petition, 9F7523, proposing the establishment of a tolerance for "combined" residues of the herbicide thifensulfuron methyl (with the CAS name of methyl-3-[[[[(4-methoxy-6-methyl-1, 3, 5-triazin-2-yl)amino] carbonyl] amino] sulfonyl]-2-thiophenecarboxylate) in or on safflower seeds, the raw agricultural commodity (RAC), as listed below.

Safflower, seed.....0.05 ppm

The end-use product (EP) proposed for use on safflower is DuPont™ Harmony® SG Herbicide (EPA Registration #352-633), a soluble granule (SG) formulation containing 50% (by weight) thifensulfuron methyl as the active ingredient (ai). Harmony® SG is proposed for one post-emergence broadcast foliar spray on safflower at a maximum application rate of 0.019 pound ai per acre (lb ai/A), with a pre-harvest interval (PHI) of 81 days. Application may be made up to the time of flower bud initiation, using ground or aerial equipment, with adjuvants in the spray mixture. The proposed use is limited to safflower grown in the states of North Dakota, South Dakota, Nebraska, Montana (East of Route 87 or East of I-15), and Wyoming (East of I-25 or North of I-90).

Tolerances for residues of thifensulfuron methyl are listed under 40CFR §180.439[a]. Permanent tolerances are established for thifensulfuron methyl in/on barley, canola, corn, cotton, flax, oat, rice, sorghum, soybean, and wheat commodities, at levels ranging from 0.02 to 2.5 ppm. No tolerances are currently established for residues in animal commodities or rotational crops.

The nature of the residue in plants is adequately understood, based on acceptable studies with wheat, corn and soybeans. The metabolism of thifensulfuron methyl in tested crops proceeds by hydrolysis of the methyl ester and sulfonyl urea moieties, with some demethylation of the triazine methoxy group. HED has previously determined that the residue of concern (ROC) in plant commodities is thifensulfuron methyl for the purposes of tolerance enforcement, and risk assessment. The available plant metabolism studies are adequate to support the requested use on safflower.

The nature of the residue in livestock is adequately understood, based on the available goat metabolism study. This determination is based on the low level of transfer of thifensulfuron methyl residues to goat matrices, and the lack of detectable residues in livestock feed items, even at exaggerated application rates. HED concluded that, because no detectable residues of thifensulfuron methyl were found in registered poultry feed items, a poultry metabolism study is not required. HED has previously determined that the ROC in plant commodities is

thifensulfuron methyl for the purposes of tolerance expression, and risk assessment. The current safflower petition does not alter HED's earlier conclusions regarding livestock metabolism.

Two high performance liquid chromatography (HPLC) photo-conductivity detection methods (Methods AMR-646-86 and AMR-761-87) are available for enforcing tolerances for residues of thifensulfuron methyl in cereal grains and straw. A liquid chromatography with mass spectrometric detection (LC/MS) method (DuPont Method 1381) is also available for enforcing tolerances for residues of thifensulfuron methyl in canola, cotton and flax commodities; the validated limit of quantitation (LOQ) for this method is 0.020 ppm. The LC/MS method will be suitable for enforcing the proposed tolerance in safflower seed. The FDA multiresidue methods are not suitable for tolerance enforcement, as thifensulfuron methyl is not recovered through any of the FDA Multiresidue Method Testing protocols. Samples collected from the safflower field trial and processing studies were analyzed for residues of thifensulfuron methyl using an HPLC photo-conductivity method (DuPont Method AMR-973-87). The method was adequate for data collection based on acceptable method validation and concurrent method recoveries.

The available storage stability data adequately support the sample storage durations and conditions incurred during the safflower field trial and processing studies. No storage stability corrections need to be applied to the safflower field trial and processing study results.

According to *OPPTS Residue Chemistry Test Guideline 860.1000*, Table 1 Feedstuffs (June 2008), safflower meal is the only animal feedstuff associated with the current petition. Safflower meal may constitute up to 5% of beef cattle diet, 10% of dairy cattle diet, 25% of poultry diet, and 5% of swine diet. In consideration of the proposed regional use of thifensulfuron methyl on safflower, and the observed residues of <0.050 ppm in safflower meal, the potential contribution to the maximum reasonably balanced dietary burdens of livestock is negligible. Therefore, tolerances in meat, milk, poultry and eggs are not required for this petition.

The submitted residue data for safflower seeds are adequate to fulfill data requirements for the requested use in the states of North Dakota, South Dakota, Nebraska, Montana (East of Route 87 or East of I-15), and Wyoming (East of I-25 or North of I-90). The number and location of the safflower field trials support the requested regional use of Harmony® SG on safflower. The data reflect the proposed use pattern, which involves a maximum use rate of 0.019 lb ai/A, a minimum PHI of 81 days, and use of a non-ionic surfactant (NIS) in the spray mixture. HED concludes that the proposed tolerance of 0.05 ppm is appropriate.

The submitted safflower processing study showed that residues of thifensulfuron methyl were <0.050 ppm in safflower meal, and refined oil, processed from safflower seeds treated at a 1X rate. DuPont has previously submitted a processing study depicting the magnitude of thifensulfuron methyl residue in cotton seeds. Residues of thifensulfuron methyl were non-detectable (<0.006 ppm) in cotton seeds harvested at normal maturity (133 days after treatment) following a single defoliant broadcast application of the 50% ai dry flowable (DF) formulation at 0.094 lb ai/A (roughly 4X the normal use rate), made one day after planting of cotton. The requirement for processing studies in canola and flax has previously been waived, based on the results of the cotton study. Therefore, a 5X safflower processing study is not required, because residues are not expected to be found in the processed commodities.

An analytical standard for thifensulfuron methyl is currently available in the National Pesticide Standards Repository (NPSR).

Confined rotational crop studies have previously been submitted. These studies were initially reviewed by the Environmental Fate and Effects Division (EFED), and were deemed inadequate pending submission of additional data and information to upgrade the acceptability of a greenhouse confined rotational crop study with [triazine-2-^{14}C]-thifensulfuron methyl. The requested data and information have been submitted, and reviewed by HED. HED concluded that although the data are not fully adequate, a new confined rotational crop study will not be required because of the nature of the pesticide. It is unlikely that additional ROCs would be found if the study were repeated. No field rotational crop studies have been submitted for thifensulfuron methyl, and none are required for this petition. The 45-day plantback interval (PBI) on the product label for Harmony® SG is adequate.

Regulatory Recommendations and Residue Chemistry Deficiencies

Pending submission of a revised Section F, there are no major deficiencies which would preclude the establishment of a permanent tolerance for regional use of thifensulfuron methyl (as Harmony® SG) on safflower. Provided that the forthcoming human health risk assessment (D361902; W.T. Drew; 29 January 2010) does not identify any issues of concern, the submitted data support a regional tolerance for residues of thifensulfuron methyl, including its metabolites and degradates, in or on safflower seeds, at the level listed below. Compliance with the tolerance level specified below is to be determined by measuring thifensulfuron methyl only.

Safflower, seed.....0.05 ppm

The deficiency noted in this document is presented below.

860.1550 Proposed Tolerances

A revised Section F should be submitted to delete the word "combined" from the tolerance expression.

Note to RD: According to HED's *Interim Guidance on Tolerance Expressions* (S. Knizner, 27 May 2009), the tolerance expression for thifensulfuron methyl cited in 40CFR §180.439[a] should be revised to state:

> **Tolerances are established for residues of thifensulfuron methyl, including its metabolites and degradates, in or on the commodities listed in the table below. Compliance with the tolerance levels specified below is to be determined by measuring only thifensulfuron methyl (methyl 3-[[[[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)amino]carbonyl]amino] sulfonyl]-2-thiophenecarboxylate).**

Background

The chemical structure and nomenclature of thifensulfuron methyl are presented in Table 1, below. The physicochemical properties of the technical grade of thifensulfuron methyl are presented in Table 2, below.

TABLE 1 Thifensulfuron Methyl Nomenclature.

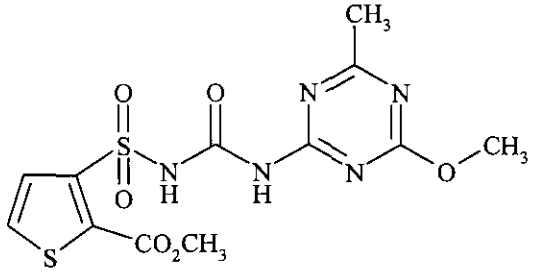
Chemical structure	
Common name	Thifensulfuron methyl
Molecular formula	$C_{12}H_{13}N_5O_6S_2$
Molecular weight	387.38
Company experimental name	DPX-M6316
IUPAC name	Methyl 3-(4-methoxy-6-methyl-1,3,5-triazin-2-ylcarbamoylsulfamoyl) thiophene-2-carboxylate
CAS name	Methyl 3-[[[[(4-methoxy-6-methyl-1,3,5- triazin-2-yl)amino]carbonyl]amino] sulfonyl]-2-thiophenecarboxylate
CAS registry number	79277-27-3
End-use product (EP)	Field trials: 75% ai DF, DuPont™ Harmony® GT XP, EPA Registration #352-446 Proposed use: 50% ai SG, DuPont™ Harmony® SG, EPA Registration #352-633

TABLE 2 Physicochemical Properties of Thifensulfuron Methyl.

Parameter	Value	Reference
Melting point/range (°C)	171.1 ± 1.2	MRID #47138301 (D342084; D. Dotson; 17 April 2008)
pH	4.0	
Density (g/cm^3)	1.58 ± 0.004	
Water solubility (g/L at 25°C)	pH 5 0.223 pH 7 2.24 pH 9 8.83	
Solvent solubility (g/L at 25°C)	Acetone - 11.9 Acetonitrile - 7.3 Dichloromethane - 27.5 Ethanol - 0.9 Ethyl acetate - 2.6 Hexane - <0.1 Methanol - 2.6 Xylene - 0.2	

TABLE 2 Physicochemical Properties of Thifensulfuron Methyl.			
Parameter	**Value**		**Reference**
Vapor pressure (25°C)	1.7×10^{-8} Pa (1.3×10^{-10} mm Hg)		
Dissociation constant (pK_a)	4.0		
Octanol/water partition coefficient (Log [K_{OW}])	pH 5 pH 7 pH 9	1.06 0.0222 0.0078	
UV/visible absorption (max, λ)	pH <2 pH 7 pH >10	224, 250 nm 233 nm 234 nm	

860.1200 Directions for Use

The EP proposed for use on safflower is DuPont™ Harmony® SG herbicide (EPA Registration #352-633), an SG formulation containing 50% thifensulfuron methyl as the ai. The proposed use directions for safflower are summarized in Table 3 (below), and were extracted from an undated supplemental label. The proposed use directions are consistent with the information provided in a revised Section B.

TABLE 3 Summary of Proposed Use of Thifensulfuron Methyl on Safflower.						
Application Timing; Type; and Equipment	**EP [EPA Registration #]**	**Use Rate (lb ai/A)**	**Max. # of Uses per Season**	**Max. Seasonal Use Rate (lb ai/A)**	**PHI (Days)**	**Use Directions and Limitations [2]**
Post-emergence (up until flower bud initiation); broadcast foliar; ground or aerial [1]	Harmony® SG, 50% ai [352-633]	0.014-0.019	1	0.019	81	Use limited to North Dakota, South Dakota, Nebraska, Montana (east of Route 87 or east of I-15), and Wyoming (east of I-25 or north of I-90). Spray adjuvants may be included with the spray treatment. [3]

1. The supplemental label does not specify application spray volumes. The approved label specifies minimum spray volumes of 10-25 gallons per acre (GPA) via ground equipment, and 5 GPA via aerial equipment for most field crops. The field trials were conducted in 15-19 GPA via ground equipment.
2. The approved label specifies the following rotational crop restrictions: Wheat, barley, oat, triticale, soybeans, and field corn may be replanted anytime after the application of Harmony® SG. Any other crop may be planted 45 days after the application of Harmony® SG.
3. Non-ionic surfactants (NISs) may be mixed with the spray mixture at a rate of 2-4 pints per 100 gallons of spray solution (concentration of 0.25-0.55% v/v). The surfactant product must contain at least 60% NIS, with a hydrophilic/lipophilic balance (HLB) greater than 12. Crop oil concentrate may be used under dry conditions or during cool weather. A petroleum-based oil concentrate may be used in place of an NIS at 1-2% (v/v). Use an oil adjuvant that contains at least 80% of a high quality, petroleum (mineral) or modified vegetable seed oil with at least 15% surfactant emulsifiers.

Conclusions: The proposed label directions for Harmony® SG are adequate to allow evaluation of the residue data. Although the submitted magnitude of the residue study for safflower reflects the use of a 75% ai dry flowable (DF) formulation (as opposed to the requested 50% ai SG formulation), the field trials reflect the proposed use rate, and PHI.

860.1300 Nature of the Residue - Plants

Residue Chemistry Memo D342084; D. Dotson; 17 April 2008 (PP#7F7219)
Residue Chemistry Memo D301509; J. Facey; 10 June 2004 (Metabolism Decision Document)

The nature of the residue in plants is adequately understood, based on acceptable studies with wheat, corn and soybeans. The salient features of these metabolism studies were recently summarized in a residue chemistry summary document (D342084; D. Dotson; 17 April 2008). The metabolism of thifensulfuron methyl in tested crops proceeds by hydrolysis of the methyl ester and sulfonyl urea moieties, with some demethylation of the triazine methoxy group. HED has determined that the ROC in plant commodities is thifensulfuron methyl for the purposes of tolerance expression, and risk assessment. The available plant metabolism studies are adequate to support the requested use on safflower.

860.1300 Nature of the Residue - Livestock

Residue Chemistry Memo D342084; D. Dotson; 17 April 2008 (PP#7F7219)
Residue Chemistry Memo D301509; J. Facey; 10 June 2004 (Metabolism Decision Document)

The nature of the residue in livestock is adequately understood, based on the available goat metabolism study. HED has previously concluded in D342084 that the goat metabolism study is adequate in supporting the registered uses of thifensulfuron methyl residues on cereal grains, and soybeans. This conclusion is based on the low level of transfer of thifensulfuron methyl residues to goat matrices, and the lack of detectable residues in livestock feed items, even at exaggerated application rates. HED also concluded that, because no detectable residues of thifensulfuron methyl were found in poultry feed items, a poultry metabolism study is not required. HED has determined that the ROC in livestock commodities is thifensulfuron methyl for the purposes of tolerance expression, and risk assessment. The current petition does not alter HED's earlier conclusions regarding livestock metabolism.

860.1340 Residue Analytical Methods

Residue Chemistry Memo D342084; D. Dotson; 17 April 2008 (PP#7F7219)
Residue Chemistry Memo D311607; S. Ary; 4 January 2005
Residue Chemistry Memo D301488; S. Ary; 12 August 2004
Residue Chemistry Memo D301509; J. Facey; 10 June 2004 (Metabolism Decision Document)

Enforcement methods: Two HPLC photo-conductivity detection methods (Methods AMR-646-86 and AMR-761-87) are available for enforcing tolerances for residues of

thifensulfuron methyl in cereal grains and straw. For Method AMR-646-86, straw samples are extracted with ethyl acetate, and the extract is partitioned with sodium bicarbonate. The aqueous phase is acidified, and partitioned with dichloromethane. The dichloromethane phase is evaporated to dryness, and then reconstituted for analysis via HPLC with photo-conductivity detection. For Method AMR-761-87, wheat grain is extracted with ethyl acetate, barley grain is extracted with 0.1 M sodium bicarbonate, and straw is extracted with ethyl acetate/HCl (at pH 3). Extracts are then analyzed via HPLC with photo-conductivity detection.

An LC/MS method (DuPont Method 1381) is also available for enforcing tolerances for residues of thifensulfuron methyl in canola, cotton, and flax commodities. For this method, samples are extracted with an acetonitrile/ammonium carbonate buffer solution, and the concentrated residues are reconstituted in methanol for analysis. If required, a hexane wash step, or cleanup step using a strong anion exchange solid phase extraction (SPE) column, may be incorporated. Analysis is performed via column-switching LC. Extracts in methanol are applied to a size exclusion chromatography column, and the eluate is diverted onto a reversed phase XDB-C_8 column for MS analysis. The validated LOQ was 0.020 ppm. This method may also be used for enforcing tolerances in corn grain, sorghum grain, and soybean seeds.

Data collection method: Samples collected from the safflower field trial and processing studies were analyzed for residues of thifensulfuron methyl using an HPLC photo-conductivity method (DuPont Method AMR-973-87). The method was adequate for data collection, based on acceptable method validation and concurrent method recoveries. Fortification levels were adequate to bracket residues found in treated samples. The lowest limit of method validation (LLMV) was 0.050 ppm in each matrix. The calculated LOQs were 0.027 ppm in safflower seeds, 0.039 ppm in meal, and 0.0068 ppm in oil. The calculated limits of detection (LODs) were 0.009 ppm in seeds, 0.013 ppm in meal, and 0.0023 ppm in oil.

Conclusions: The available residue analytical method data are adequate to satisfy data requirements. The existing tolerance enforcement methods, AMR-646-86, AMR-761-87, and DuPont Method 1381, are adequate to enforce the proposed tolerance in safflower seeds, and DuPont Method AMR-973-87 is adequate for data collection purposes.

860.1360 Multiresidue Methods

Residue Chemistry Memo D301488; S. Ary; 12 August 2004
Residue Chemistry Memo CB2354; C. Deyrup; 10 March 1988

The FDA's *PESTDATA* database, dated June 2005 (*PAM Volume I*, Appendix I) does not contain any information regarding the recovery of thifensulfuron methyl using multiresidue methods. Data investigating the behavior of thifensulfuron methyl using the FDA Multiresidue Methods have been submitted by the petitioner (MRID #40429701). Because thifensulfuron methyl is thermally labile, only Multiresidue Protocol A was investigated. It was determined that thifensulfuron methyl does not give a sufficient response on the required HPLC system (D301488; S. Ary; 12 August 2004). The available data indicate that residues of thifensulfuron methyl are not recovered by the FDA multiresidue methods.

860.1380 Storage Stability

Residue Chemistry Memos D330702 and D330813; S. Hummel; 8 August 2006
Residue Chemistry Memo D301488; S. Ary; 12 August 2004
Residue Chemistry Memo PP#8G3602; R. Loranger; 18 May 1988
Residue Chemistry Memo PP#6F3431; C. Deyrup; 24 December 1987

The storage durations and conditions of commodity samples collected from the safflower field trial and processing studies are listed in Table 4, below. To validate sample storage conditions and durations, a concurrent storage stability study was conducted. Control samples of safflower seeds, meal and oil were fortified with thifensulfuron methyl at 0.10 ppm, followed by frozen storage of the fortified samples for the duration of the analysis of the field trial samples. At the end of the analytical phase, the storage stability samples were analyzed for residues of thifensulfuron methyl. The overall average corrected recoveries were 92% from safflower seeds, 97% from safflower meal, and 108% from safflower oil. Although there was no zero-day analysis of fortified samples, the storage stability data are adequate, and support the storage conditions and durations incurred in the field trial and processing studies.

TABLE 4 Summary of Storage Conditions and Durations of Samples from the Safflower Field Trial and Processing Studies.

Matrix	Storage Temperature (°C)	Actual Storage Duration (Days)	Interval of Demonstrated Storage Stability (Days)
Safflower seeds	-26 to -14	608-632	631
Safflower meal		567	584
Safflower oil		561	588

Additional storage stability data are available from previous submissions. These data indicate that thifensulfuron methyl is stable under frozen storage conditions for intervals of at least 4 months in corn stover and soybean seeds, 14 months in cotton seeds and cotton gin byproducts, 24 months in corn grain and forage, and wheat straw, and 36 months in wheat grain.

Conclusions: The available storage stability data adequately support the sample storage durations incurred in the safflower field trial and processing studies. No storage stability corrections need to be applied to the safflower field trial and processing study results.

860.1400 Water, Fish, and Irrigated Crops

There are no proposed or registered uses that are relevant to this guideline topic.

860.1460 Food Handling

There are no proposed or registered uses that are relevant to this guideline topic.

860.1480 Meat, Milk, Poultry, and Eggs

According to *OPPTS Residue Chemistry Test Guideline 860.1000*, Table 1 Feedstuffs (June 2008), safflower meal is the only animal feedstuff associated with the current petition. Safflower meal may constitute up to 5% of beef cattle diet, 10% of dairy cattle diet, 25% of poultry diet, and 5% of swine diet. In consideration of the proposed regional use of thifensulfuron methyl on safflower, and the observed residues of <0.050 ppm in safflower meal, the potential contribution to the maximum reasonably balanced dietary burdens of livestock is negligible. Therefore, tolerances in meat, milk, poultry and eggs are not required for this petition.

860.1500 Crop Field Trials

DER for MRID #47641801 (CFTs with Safflower)

Three safflower field trials were conducted in Zones 5 (SD) and 7 (ND; 2 trials) during the 2000 growing season. At each site a 75% ai DF formulation of thifensulfuron methyl was applied to safflower as a single broadcast foliar application, either 81 or 36 days prior to harvest, at rates of 0.0176-0.0187 lb ai/A (roughly 1X the proposed rate). Applications were made using ground equipment, in spray volumes of 15-19 GPA, and included the use of an NIS adjuvant. Duplicate control and treated samples of safflower were harvested 81 days after treatment (DAT) from two ND field trials, and 36 DAT from the SD field trial.

Samples of safflower seeds were analyzed for residues of thifensulfuron methyl using an adequate HPLC photo-conductivity method (DuPont Method AMR-973-87). The method was adequate for data collection, based on acceptable method validation and concurrent method recoveries. Fortification levels were adequate to bracket residues found in treated samples. The LLMV was 0.050 ppm, while the calculated LOQ and LOD were 0.027 and 0.009 ppm, respectively.

Safflower seed samples were stored for up to 632 days prior to analysis. The sample storage conditions and durations for safflower seeds are supported by adequate concurrent storage stability data.

The results indicate that following one broadcast foliar application of thifensulfuron methyl (75% ai DF) to safflower, at rates of 0.0176-0.0187 lb ai/A, residues in safflower seeds were <0.050 ppm for all 6 samples harvested at either 81 DAT or 36 DAT (see Table 5, below). Although the treatment rate at the SD trial was under-applied by 7%, and samples were harvested more than 40 days earlier than the other field trials, this application error will have no impact on the adequacy of the field trials, as all residues were <0.050 ppm. A residue decline study was not conducted.

TABLE 5 Summary of Residue Data from Safflower Field Trials with Thifensulfuron Methyl.									
Commodity	Total Use Rate (lb ai/A)	PHI (Days)	Residue Levels (ppm)						
			n	Min.	Max.	HAFT*	Median	Mean	Std. Dev.
Safflower Seed	0.0176-0.0187	36-81	6	<0.05	<0.05	<0.05	<0.05	<0.05	0

* HAFT = Highest Average Field Trial result.

Conclusions: The residue data for safflower seeds are adequate to fulfill data requirements for the proposed use. Although the field trials were conducted with a 75% ai DF formulation of thifensulfuron methyl, the number and location of the field trials support the requested regional use of Harmony® SG on safflower. The data reflect the proposed use pattern (maximum use rate of 0.019 lb ai/A, a PHI of 81 days, and use of an NIS in the spray mixture). HED concludes that the proposed tolerance of 0.05 ppm is appropriate.

860.1520 Processed Food and Feed

DER for MRID #47641801 (PFF from Safflower Seeds)

To generate samples to be used for processing, one trial was conducted in ND during the 2000 growing season. Safflower seeds were harvested 81 days following a single broadcast foliar application of the 75% ai DF formulation, at a rate of 0.0186 lb ai/A (roughly 1X the proposed rate). The application was made using ground equipment in a spray volume of 15 GPA, and included the use of an NIS. The safflower seed samples were processed into meal and refined oil using simulated commercial practices.

Samples of safflower seed, meal and refined oil were analyzed for residues of thifensulfuron methyl using an adequate HPLC photo-conductivity method (DuPont Method AMR-973-87). The method was adequate for data collection, based on acceptable method validation and concurrent method recoveries. Fortification levels were adequate to bracket residues found in treated samples. The LLMV in each matrix was 0.050 ppm. The calculated LOQs were 0.027 ppm in seed, 0.039 ppm in meal, and 0.0068 ppm in oil, while the calculated LODs were 0.009 ppm in seed, 0.013 ppm in meal, and 0.0023 ppm in oil.

Samples of safflower seed were stored frozen for up to 608 days, while processed samples of meal and oil were stored frozen for up to 567 and 561 days, respectively, prior to analysis. The storage durations are supported by adequate storage stability data, which were generated concurrently with the safflower field trial and processing studies.

Residues of thifensulfuron methyl were below the LLMV (<0.050 ppm) in safflower seed RAC samples harvested 81 days after treatment at a rate of 0.0186 lb ai/A (1X the field trial application rate). Following processing, residues of thifensulfuron methyl were <0.050 ppm in safflower meal and refined oil processed from treated safflower seed. Processing factors could not be calculated because residues were below the LLMV in both the RAC and the processed fractions. The theoretical processing factors for safflower meal and oil are 9.1X and 3.3X, respectively (*OPPTS Residue Chemistry Test Guideline 860.1520*, Table 3).

Conclusions: The submitted safflower processing study showed that residues of thifensulfuron methyl were <0.050 ppm in safflower meal, and refined oil, processed from safflower seeds treated at 1X. Thifensulfuron methyl is not expected to concentrate in safflower oil because it has a very low octanol/water partition coefficient (Log K_{OW} = 0.027). It has been shown in the cotton processing study (MRID #45098405) that, after treatment at an exaggerated rate of 0.094 lb ai/A (roughly 4X the normal use rate of 0.025 lb ai/A), applied one day after planting, with a 133-day PHI, residues of thifensulfuron methyl were non-detectable (<0.006 ppm) in undelinted cotton seeds. As with cotton, the PHI for safflower following treatment with thifensulfuron methyl is relatively long (81 days). Cotton seeds, like safflower seeds, may be processed into oil or meal, and as such, thifensulfuron methyl is not expected to concentrate in safflower processed food/feed items. Also, the requirement for processing studies in canola and flax has previously been waived, based on the results of the cotton study. Therefore, a 5X processing study is not required in safflower.

860.1650 Submittal of Analytical Reference Standards

An analytical standard for thifensulfuron methyl is currently available in the NPSR, via personal communication with Dallas Wright, of the Biological and Economic Analysis Division's Analytical Chemistry Branch (BEAD/ACB), on 27 July 2009. Analytical reference standards should be replenished as requested by the Repository. The reference standards should be sent to the ACB, which is located at Fort Meade, to the attention of Theresa Cole at the following address:

USEPA
National Pesticide Standards Repository/Analytical Chemistry Branch/OPP
701 Mapes Road
Fort George G. Meade, MD 20755-5350

(Note that the mail will be returned if the extended zip code is not used.)

860.1850 Confined Accumulation in Rotational Crops
860.1900 Field Accumulation in Rotational Crops
Residue Chemistry Memo D342084; D. Dotson; 17 April 2008 (PP#7F7219)

Confined rotational crop studies have previously been submitted. These studies were initially reviewed by EFED, and were deemed inadequate pending submission of additional data and information to upgrade the acceptability of a greenhouse confined rotational crop study with [triazine-2-^{14}C]-thifensulfuron methyl. The requested data and information have been submitted and reviewed by HED. HED concluded that although the data are not fully adequate, a new confined rotational crop study will not be required because of the nature of the pesticide. It is unlikely that additional ROCs would be found if the study were repeated. No field rotational

crop studies have been submitted for thifensulfuron methyl, and none are required for this petition. The 45-day PBI on the product label for Harmony® SG is adequate.

860.1550 Proposed Tolerances

HED has previously determined that the ROC in plant commodities is thifensulfuron methyl for the purposes of tolerance expression, and risk assessment. Permanent tolerances are established for thifensulfuron methyl in/on barley, canola, corn, cotton, flax, oat, rice, sorghum, soybean and wheat commodities, at levels ranging from 0.02 to 2.5 ppm (40CFR §180.439[a]). The subject petition proposes a tolerance for "combined" residues of the herbicide thifensulfuron methyl in/on safflower, seed (RAC) at 0.05 ppm. A revised Section F should be submitted to delete the word "combined" from the tolerance expression.

The safflower field trial data are adequate to support a regional tolerance of 0.05 ppm in safflower seeds grown in North Dakota, South Dakota, Nebraska, Montana (east of Route 87 or east of I-15), and Wyoming (east of I-25 or north of I-90). All safflower seeds bore residues below the LLMV (<0.050 ppm) following application of a 75% ai DF formulation according to the proposed rate and PHI. No tolerances are required for residues of thifensulfuron methyl in animal commodities, nor in rotational crops, for the purposes of this petition.

A summary of the proposed and recommended tolerances is presented in Table 6, below.

There are no established or proposed Codex Maximum Residue Limits (MRLs) for residues of thifensulfuron methyl. Canada and Mexico have established MRLs for thifensulfuron methyl in several plant commodities. The ROCs in Canada, Mexico and the US are harmonized. However, no Canadian or Mexican MRLs for thifensulfuron methyl have been proposed or established in safflower seed. An International Residue Limit Status sheet is appended to this document.

TABLE 6 Tolerance Summary for Thifensulfuron Methyl.

Commodity	Proposed Tolerance (ppm)	Recommended Tolerance (ppm)	Comments; *Correct Commodity Definition*
Safflower, seed	0.05	0.05	

References

PP #7F7219 Label Amendments and Petition for Tolerances on Wheat Forage and Hay, Oat Forage and Hay, and Barley Hay. Summary of Analytical Chemistry and Residue Data.; D342084; D. Dotson; 17 April 2008.

Thifensulfuron Methyl. Addition of Uses on Rice and Sorghum (PRIA R19 - 352-611; PP#4F6889). Summary of Analytical Chemistry and Residue Data.; D330702 and D330813; S. Hummel; 8 August 2006.

Thifensulfuron Methyl. HED's Response to E.I. du Pont de Nemours and Company's Comments to the "Summary of Residue Chemistry Data Evaluation Records for the Establishment of Tolerances for New Uses of Thifensulfuron Methyl on Canola, Flax, and Cotton."; D311607; S. Ary; 4 January 2005.

Thifensulfuron Methyl. Summary of Residue Chemistry Data Evaluation Records for the Establishment of Tolerances for New Uses of Thifensulfuron Methyl on Canola, Flax, and Cotton.; D301488; S. Ary; 12 August 2004.

Thifensulfuron Methyl. Meeting Report of the Metabolism Assessment Review Committee Document. TXR Number 0052419; D301509; J. Facey; 10 June 2004.

PP#8G3602, 352-EUP-RUL. DPX-M316 (Pinnacle) on Soybeans. Evaluation of Analytical Method and Residue Data; R. Loranger; 18 May 1988.

PP #6F3431. Response (2 December 1987) by E.I. Du Pont de Nemours & Co. to the Need for Testing DPX-H6573 (Harmony™) with Multiresidue Protocols. (RCB #22354); CB2354; C. Deyrup; 10 March 1988.

PP #6F3431. Response (14 September 1987) by E.I. Du Pont de Nemours & Co. to the Data Gaps Identified in the Product Chemistry Chapter and Residue Chemistry Chapter of the 2/87 Harmony (DPX-M6316) Registration Standard. (RCB #2825); C. Deyrup; 24 December 1987.

Appendix 1 - International Residue Limit Status Sheet

INTERNATIONAL RESIDUE LIMIT STATUS

CAS Name: 3-[[[[(4-methoxy-6-methyl-1,3,5-triazin-2-yl) amino]carbonyl]amino] sulfonyl]-2-thiophenecarboxylic acid	**Common Name:** Thifensulfuron methyl	**X Proposed tolerance** ☐ Reevaluated tolerance ☐ Other	**Date:** 27 July 2009

Codex Status (Maximum Residue Limits)		**US Tolerances**	
X No Codex proposal step 6 or above ☐ No Codex proposal step 6 or above for the crops requested		Petition Number: 9F7523 DP Barcode: D361945 Other Identifier: PC Code 128845	
Residue definition (step 8/CXL):		Reviewer/Branch: William T. Drew/RAB2	
		Residue definition: Thifensulfuron methyl	
Crop(s)	MRL (mg/kg)	Crop	Tolerance (ppm)
		Safflower, seed	0.05

Limits for Canada		**Limits for Mexico**	
☐ No Limits X No Limits for the crops requested		☐ No Limits X No Limits for the crops requested	
Residue definition: Methyl-3-[[[[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)amino]carbonyl]amino]sulfonyl]-2-thiophenecarboxylate		Residue definition: Thifensulfron methyl	
Crop(s)	MRL (mg/kg)	Crop(s)	MRL (mg/kg)

Notes and/or special instructions: per Steve Funk, 27 July 2009.

Thifensulfuron Methyl/352-633/PC Code 128845/Interregional Research Project #4
DACO 7.4.1/7.4.2/OPPTS 860.1500/OECD IIA 6.3.1, 6.3.2, 6.3.3 and IIIA 8.3.I, 8.3.2, 8.3.3
Crop Field Trial – Safflower (Seed)

Primary Evaluator — William T. Drew, Chemist, HED/RAB2 — Date: 29 September 2009

Peer Reviewer — Dennis McNeilly, Chemist, HED/RAB2 — Date: 6 October 2009

This data evaluation record (DER) was originally prepared under contract by Dynamac Corporation (1910 Sedwick Road, Building 100, Suite B; Durham, NC 27713). The DER has been reviewed by the Registration Division (RD) and the Health Effects Division (HED), and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT

MRID #47641801. Frederick P. Salzman (2007) *Thifensulfuron-Methyl: Magnitude of Residue on Safflower.* IR-4 Project Number A3454. Analytical Laboratory Identification Number A3454.00-NDR03. Unpublished study prepared by IR-4. 171 pages.

EXECUTIVE SUMMARY

The Interregional Research Project Number 4 (IR-4) has submitted field trial data for thifensulfuron methyl on safflower. Three safflower field trials were conducted in Zones 5 (SD) and 7 (ND; 2 trials) during the 2000 growing season. At each site, a dry flowable (DF) formulation of thifensulfuron methyl, containing 75% active ingredient (ai), was applied to safflower as a single broadcast foliar application, either 81 or 36 days prior to harvest, at rates of 0.0176-0.0187 pound ai per acre (lb ai/A). Applications were made using ground equipment, in spray volumes of 15-19 gallons per acre (GPA), and included the use of a non-ionic surfactant (NIS). Duplicate control and treated samples of safflower were harvested 81 days after treatment (DAT) from the two ND field trials, and 36 DAT from the SD field trial.

Samples of safflower seeds were analyzed for residues of thifensulfuron methyl using an adequate high performance liquid chromatography (HPLC) photo-conductivity method (DuPont Method AMR-973-87). The method was adequate for data collection, based on acceptable method validation and concurrent method recoveries. Fortification levels were adequate to bracket residues found in treated samples. The lowest limit of method validation (LLMV) was 0.050 ppm, while the calculated limit of quantitation (LOQ), and limit of detection (LOD) were 0.027 and 0.009 ppm, respectively.

Safflower seed samples were stored for up to 632 days prior to analysis. The sample storage conditions and durations for safflower seeds are supported by adequate concurrent storage stability data.

Following one broadcast foliar application of thifensulfuron methyl (75% ai DF) to safflower, at rates of 0.0176-0.0187 lb ai/A, residues in safflower seeds were <0.050 ppm for all 6 samples harvested at either 81 DAT or 36 DAT (Tables C.3 and C.4). Although the application rate at the SD trial was under-applied by 7%, and samples were harvested more than

40 days earlier than the other field trials, this application error will have no impact on the adequacy of the field trial samples, as all residues were <0.050 ppm. A residue decline study was not conducted.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS

Under the conditions and parameters used in the study, the safflower field trial residue data are classified as scientifically acceptable. The acceptability of this study for regulatory purposes is addressed in the US EPA Residue Chemistry Summary Document, D361945.

COMPLIANCE

Signed and dated Good Laboratory Practice (GLP), Quality Assurance, and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an adverse impact on the validity of the study.

A. BACKGROUND INFORMATION

Thifensulfuron-methyl is a sulfonylurea herbicide (Group 2) registered for post-emergence application to barley, canola, cotton, flax, field corn, oat, soybean and wheat for selective control of broadleaf weeds. It is absorbed through the foliage of treated weeds, inhibiting growth, causing necrosis of the growing plant, and eventual plant death. Permanent tolerances are established for thifensulfuron methyl in/on barley, canola, corn, cotton, flax, oat, rice, sorghum, soybean and wheat commodities, at levels ranging from 0.02 to 2.5 ppm (40CFR §180.439[a]).

For the current petition (9F7523), IR-4 is proposing a new use for thifensulfuron methyl on safflower. The chemical structure and nomenclature of thifensulfuron methyl are presented in Table A.1, below. The physicochemical properties of the technical grade of thifensulfuron methyl are presented in Table A.2, below.

TABLE A.1 Thifensulfuron Methyl Nomenclature.

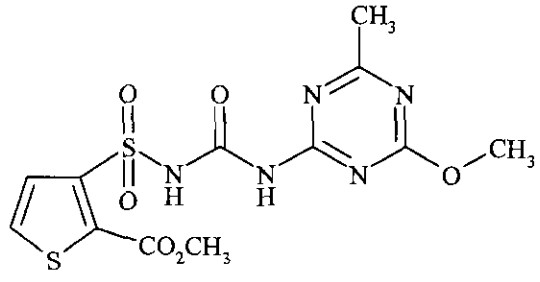
Chemical structure	

TABLE A.1 Thifensulfuron Methyl Nomenclature.	
Common name	Thifensulfuron methyl
Molecular formula	$C_{12}H_{13}N_5O_6S_2$
Molecular weight	387.38
Company experimental name	DPX-M6316
IUPAC name	Methyl 3-(4-methoxy-6-methyl-1,3,5-triazin-2-ylcarbamoylsulfamoyl) thiophene-2-carboxylate
CAS name	Methyl 3-[[[[(4-methoxy-6-methyl-1,3,5- triazin-2-yl)amino]carbonyl]amino] sulfonyl]-2-thiophenecarboxylate
CAS registry number	79277-27-3
End-use product (EP)	Field trials: 75% ai DF, DuPont™ Harmony® GT XP, EPA Registration #352-446 Proposed use: 50% ai SG, DuPont™ Harmony® SG, EPA Registration #352-633

TABLE A.2 Physicochemical Properties of Thifensulfuron Methyl.		
Parameter	**Value**	**Reference**
Melting point/range (°C)	171.1 ± 1.2	MRID #47138301 (D342084; D. Dotson; 17 April 2008)
pH	4.0	
Density (g/cm^3)	1.58 ± 0.004	
Water solubility (g/L at 25°C)	pH 5 0.223 pH 7 2.24 pH 9 8.83	
Solvent solubility (g/L at 25°C)	Acetone - 11.9 Acetonitrile - 7.3 Dichloromethane - 27.5 Ethanol - 0.9 Ethyl acetate - 2.6 Hexane - <0.1 Methanol - 2.6 Xylene - 0.2	
Vapor pressure (25°C)	1.7 x 10^{-8} Pa (1.3 x 10^{-10} mm Hg)	
Dissociation constant (pK_a)	4.0	
Octanol/water partition coefficient (Log [K_{OW}])	pH 5 1.06 pH 7 0.0222 pH 9 0.0078	
UV/visible absorption (max, λ)	pH <2 224, 250 nm pH 7 233 nm pH >10 234 nm	

B. EXPERIMENTAL DESIGN

B.1. Study Site Information

Three safflower field trials were conducted in Zones 5 (SD) and 7 (ND; 2 trials) during the 2000 growing season. Trial site conditions are presented in Table B.1.1, below. The crop varieties grown are identified in Table C.3, below.

At each site, a 75% ai DF formulation of thifensulfuron methyl was applied to safflower as a single broadcast foliar application, either 81 or 36 days prior to harvest, at rates of 0.0176-0.0187 lb ai/A. Applications were made using ground equipment in spray volumes of 15-19 GPA, and included the use of an NIS. Actual trial parameters are reported in Table B.1.2, below.

TABLE B.1.1 Trial Site Conditions.

Location (City, State; Year) [Trial ID]	Soil Characteristics			
	Type	%OM	pH	CEC (meq/g)
Williston, ND; 2000 [ND11]	Loam	1.7	5.9	NR*
Williston, ND; 2000 [ND12]	Loam	2.2	5.9	NR
Brookings, SD; 2000 [SD01]	Clay Loam	3.2	5.9	NR

* NR = Not Reported.

Temperature recordings, and rainfall averages were reported to be within average historical values for the field trial study period, with the exception of the SD trial site where rainfall was below normal. Irrigation was not used at any of the trial sites. The trials were conducted according to normal agricultural practices for the different regions, and information was provided on maintenance pesticides, and fertilizers used, at each location. Phytotoxic effects were noted in both ND trials; plants were reported to be a lighter green compared to plants in the untreated plots. After 10 days the proper color returned, and plants in the treated plots showed no other visible injury symptoms.

TABLE B.1.2 Study Use Pattern.

Location (City, State; Year) [Trial ID]	EP[1]	Application Information					Adjuvants
		Method; Timing	Volume (GPA)	Single Rate (lb ai/A)	RTI[2] (Days)	Total Rate (lb ai/A)	
Williston, ND; 2000 [ND11]	75% ai DF	One broadcast foliar application; late vegetative to early bud.	15	0.0187	--	0.0187	NIS
Williston, ND; 2000 [ND12]	75% ai DF	One broadcast foliar application; late vegetative to early bud.	15	0.0186	--	0.0186	NIS
Brookings, SD; 2000 [SD01]	75% ai DF	One broadcast foliar application; during bloom.	19	0.0176	--	0.0176	NIS

1. EP = End-use Product (75% ai DF = Harmony® GT XP herbicide, EPA Registration #352-446).
2. RTI = Re-Treatment Interval (not relevant to this study, as only one treatment was applied to safflower).

TABLE B.1.3. Trial Numbers and Geographical Locations.			
NAFTA Growing Zones	Safflower		
	Submitted	Requested*	
		Canada	US
1			
1A			
2			
3			
4			
5	1		
5A			
5B			
6			
7	2		2
7A			
8			
9			
10			3
11			
12			
13			
14			
Total	**3**		**5**

* *OPPTS Residue Chemistry Test Guideline 860.1500* requires five trials for safflower. The regional distribution listed in this table is suggested, not required. This study was intended to support a regional label, for use in the northern Great Plains, that only includes the northwest portion of Region 5, and all of Region 7.

B.2. Sample Handling and Preparation

Duplicate control and treated samples of safflower seeds were harvested 81 DAT from the two ND field trials, and 36 DAT from the SD field trial. Samples were placed into frozen storage within 0.5-2.1 hours, and stored frozen at the field trial sites for 2-14 days prior to shipment (by ACDS freezer truck) to the analytical facility (North Dakota IR-4 Satellite Laboratory in Fargo, ND). At the laboratory, all samples were ground and stored frozen (-24 to -14°C) until extraction and analysis.

B.3. Analytical Methodology

Samples were analyzed for residues of thifensulfuron methyl using an HPLC photo-conductivity detection method (DuPont Method AMR-973-87), entitled *A Method for Analysis of the Herbicide, DPX-M6316 in Soybeans by Liquid Chromatography*. A description of the method was included in the safflower field trial submission.

For this method, residues were extracted from safflower seeds by soaking ground seeds in 0.05 M sodium bicarbonate for a minimum of 2 hours, then adjusting the pH to 3.5 prior to

homogenization in dichloromethane (DCM). The organic solvent was isolated, and extracted three times with 0.05 M $NaHCO_3$. The resulting aqueous extracts were combined, rinsed with hexane, and adjusted to pH 3.0-3.5 with HCl. The acidic solution was cleaned up on a C_{18} solid phase extraction (SPE) cartridge; residues were eluted with methanol/0.1% acetic acid in water (3:2, v:v). The analyte was then partitioned into DCM, evaporated to dryness, and reconstituted with DCM prior to loading onto a CN SPE cartridge. The analyte was eluted with 10% ethyl acetate in DCM (v:v). The eluate was evaporated to dryness, and reconstituted in n-hexane/isopropyl alcohol (3:1, v:v) prior to analysis via HPLC with photo-conductivity detection.

The LLMV was 0.050 ppm, the calculated LOQ was 0.027 ppm, and the calculated LOD was 0.009 ppm. The method was adequately validated prior to, and in conjunction with, the analysis of the field trial samples.

To support sample storage conditions and durations, a concurrent storage stability study was conducted. Three samples of untreated safflower seeds were fortified with thifensulfuron methyl at 0.10 ppm, and then stored frozen for 631 days.

C. RESULTS AND DISCUSSION

Sample storage conditions and durations for safflower seeds are summarized in Table C.2.1, below. Safflower seed samples were stored frozen from harvest to analysis for up to 632 days. The results of the concurrent storage stability study are presented in Table C.2.2, below. These data demonstrate that residues of thifensulfuron methyl are stable in fortified safflower seeds stored frozen for intervals of up to 631 days. The average corrected recovery was 92% from safflower seeds. Zero-day data were not provided; IR-4 is reminded that storage stability studies should always include a zero-day sampling interval to establish the residue levels present at the time samples are placed into storage (see *OPPTS Residue Chemistry Test Guideline 860.1380[d][6][i]*). The concurrent storage stability data are adequate to support the storage durations and conditions of samples from the safflower field trials.

Method validation and concurrent method recovery data are presented in Table C.1, below. The HPLC photo-conductivity detection method (Method AMR-973-87) used for determining residues of thifensulfuron methyl in safflower seeds was adequately validated prior to, and in conjunction with, the analysis of field trial samples. Samples of safflower seeds were fortified with thifensulfuron methyl at 0.050-0.50 ppm for method validation, and at 0.050-0.10 ppm for concurrent analysis. The concurrent recovery fortification levels adequately bracketed the field trial residue results. Recoveries were within the generally recognized acceptable range of 70-120% from all samples. For method validation, the average recovery was 84% with a standard deviation of 6%, and for concurrent validation, the average recovery was 81% with a standard deviation of 6%. Apparent residues of thifensulfuron methyl were below the LLMV (<0.050 ppm) in six samples of untreated safflower seeds. Adequate sample calculations and chromatograms were provided.

Following one broadcast foliar application of thifensulfuron methyl (75% ai DF) to safflower, at rates of 0.0176-0.0187 lb ai/A, residues in safflower seeds were <0.050 ppm for all 6 samples harvested at either 81 DAT or 36 DAT (Tables C.3 and C.4, below). Although the application rate at the SD trial was under-applied by 7%, and samples were harvested more than 40 days earlier than the other field trials, this application error will have no impact on the adequacy of the field trial samples, as all residues were <0.050 ppm. A residue decline study was not conducted.

Common cultural practices were used to maintain plants, and the weather conditions, maintenance chemicals, and fertilizer used in the study did not have a notable impact on the residue data.

TABLE C.1 Summary of Method Validation and Concurrent Recoveries of Thifensulfuron Methyl from Safflower Seeds.

Matrix	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. [1] (%)
Method Validation				
Safflower seeds	0.050	6	82, 79, 81, 94, 90, 89	86 ± 6
	0.50	3	76, 79, 85	80 ± 5
	Total	**9**	**76-94**	84 ± 6
Concurrent Recovery				
Safflower seeds	0.050	4	71, 84, 83, 87	81 ± 7
	0.10	1	81 [2]	81
	Total	**5**	**71-87**	81 ± 6

1. Standard deviation is only calculated for sample sizes n ≥ 3.
2. Storage stability concurrent recovery (refer to Table C.2.2).

TABLE C.2.1 Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration (Days)*	Interval of Demonstrated Storage Stability (Days)
Safflower seeds	-26 to -14	608-632	631

* Storage duration from harvest to analysis. Samples were analyzed within 2-4 days of extraction.

TABLE C.2.2 Stability of Thifensulfuron Methyl Residues in Safflower Seeds Following Frozen Storage.

Commodity	Spike Level (ppm)	Storage Interval (Days)	Freshly Fortified Recovery (%)	Recoveries (%)	Corrected Recovery* (%)
Safflower seeds	0.10	631	81	70, 73, 80	86, 90, 99 (92)

* Corrected for concurrent method recovery; average corrected recovery reported in parentheses.

TABLE C.3 Residue Data from Safflower Field Trials with Thifensulfuron Methyl.

Location (City, State; Year) [Trial ID]	Zone	Safflower Variety	Matrix	Total Rate (lb ai/A)	PHI (Days)	Residues (ppm)*	
Williston, ND; 2000 [ND11]	7	Mantola 2000	Seeds	0.0187	81	<0.050	<0.050
Williston, ND; 2000 [ND12]	7	Finch	Seeds	0.0186	81	<0.050	<0.050

TABLE C.3 Residue Data from Safflower Field Trials with Thifensulfuron Methyl							
Location (City, State, Year) [Trial ID]	Zone	Safflower Variety	Matrix	Total Rate 1 (lb ai/A)	PHI (Days)	Residues (ppm)*	
Brookings, SD; 2000 [SD01]	5	Montola	Seeds	0.0176	36	<0.050	<0.050

* The LLMV was 0.050 ppm, the calculated LOQ was 0.027 ppm, and the calculated LOD was 0.009 ppm.

TABLE C.4 Summary of Residue Data from Safflower Field Trials with Thifensulfuron Methyl									
Commodity	Total Use Rate (lb ai/A)	PHI (Days)	Residue Levels (ppm)						
			n	Min.	Max.	HAFT[2]	Median	Mean	Std. Dev.
Safflower seeds	0.0176-0.0187	36-81	6	<0.050	<0.050	<0.050	<0.050	<0.050	0

1. The LLMV was 0.050 ppm, the calculated LOQ was 0.027 ppm, and the calculated LOD was 0.009 ppm.
2. HAFT = Highest Average Field Trial.

D. CONCLUSION

Although the SD trial had a lower application rate, and an earlier PHI, the safflower field trial data are adequate, and support the use of one broadcast foliar application of thifensulfuron methyl to safflower, at a rate of 0.0176-0.0187 lb ai/A. Additionally, though the field trials were conducted with a 75% ai DF formulation of thifensulfuron methyl, the number and location of the field trials support the requested regional use of Harmony® SG on safflower. The available residue data support a PHI of 81 days for safflower seeds. An acceptable method was used for quantitation of thifensulfuron methyl residues in safflower seeds, and the sample storage conditions and durations are supported by adequate concurrent storage stability data.

E. REFERENCES

Ingredient: Thifensulfuron Methyl. Title: Label Amendments and Petition for Tolerances on Wheat Forage and Hay, Oat Forage and Hay, and Barley Hay. Summary of Analytical Chemistry and Residue Data.; D342084; D. Dotson; 17 April 2008.

F. DOCUMENT TRACKING

RDI: William T. Drew (29 September 2009); Dennis McNeilly (6 October 2009)
Petition Number: 9F7523
DP Number: 361945
PC Code: 128845

Thifensulfuron Methyl/352-633/PC Code 128845/Interregional Research Project #4
DACO 7.4.5/OPPTS 860.1520/OECD IIA 6.5.4 and IIIA 8.5
Processed Food and Feed – Safflower (Meal, Refined Oil)

Primary Evaluator — Date: 30 September 2009
William T. Drew, Chemist, HED/RAB2

Peer Reviewer — Date: 6 October 2009
Dennis McNeilly, Chemist, HED/RAB2

This data evaluation record (DER) was originally prepared under contract by Dynamac Corporation (1910 Sedwick Road, Building 100, Suite B; Durham, NC 27713). The DER has been reviewed by the Registration Division (RD) and the Health Effects Division (HED), and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT

MRID #47641801. Frederick P. Salzman (2007) *Thifensulfuron-Methyl: Magnitude of Residue on Safflower.* IR-4 Project Number A3454. Analytical Laboratory Identification Number A3454.00-NDR03. Unpublished study prepared by IR-4. 171 pages.

EXECUTIVE SUMMARY

The Interregional Research Project Number 4 (IR-4) has submitted a processing study with thifensulfuron methyl on safflower. In one trial conducted in ND during the 2000 growing season, safflower seeds were harvested 81 days following a single broadcast foliar application of a dry flowable (DF) formulation of thifensulfuron methyl, containing 75% active ingredient (ai). The application was made at the rate of 0.0186 pound ai per acre (lb ai/A), which was 1X the field trial application rate. The treatment was applied via ground equipment, in a spray volume of 15 gallons per acre (GPA), and included the use of a non-ionic surfactant (NIS). The safflower seed samples were processed into meal and refined oil using simulated commercial practices.

Samples of safflower seeds, meal and refined oil were analyzed for residues of thifensulfuron methyl using an adequate high performance liquid chromatography (HPLC) photo conductivity method (DuPont Method AMR-973-87). The method was adequate for data collection, based on acceptable method validation and concurrent method recoveries. Fortification levels were adequate to bracket residues found in treated samples. The lowest limit of method validation (LLMV) in each matrix was 0.050 ppm. The calculated limits of quantitation (LOQs) were 0.027 ppm in seeds, 0.039 ppm in meal, and 0.0068 ppm in oil, while the calculated limits of detection (LODs) were 0.009 ppm in seeds, 0.013 ppm in meal, and 0.0023 ppm in oil.

Samples of safflower seeds were stored frozen for up to 608 days, while processed samples of meal and oil were stored frozen for up to 567 and 561 days, respectively, prior to analysis. The storage durations are supported by adequate storage stability data, which were generated concurrently with the safflower field trial and processing studies.

Residues of thifensulfuron methyl were below the LLMV (<0.050 ppm) in safflower seed samples, the raw agricultural commodity (RAC), harvested 81 days after treatment at the rate of 0.0186 lb ai/A (1X the field trial application rate). Following processing, residues of thifensulfuron methyl were <0.050 ppm in safflower meal and refined oil processed from treated safflower seeds. Processing factors could not be calculated because residues were below the LLMV in both the RAC and the processed fractions.

The theoretical processing factors for safflower meal and refined oil are 9.1X and 3.3X, respectively (*OPPTS Residue Chemistry Test Guideline 860.1520*, Table 3).

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS

Under the conditions and parameters used in the study, the safflower processing study residue data are classified as scientifically acceptable, but inadequate. The application rate used in the study is only 1X the proposed rate. Therefore, the potential for concentration of residues in safflower processed commodities could not be reliably assessed. The acceptability of this study for regulatory purposes is addressed in the US EPA Residue Chemistry Summary Document, D361945.

COMPLIANCE

Signed and dated Good Laboratory Practice (GLP), Quality Assurance, and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an impact on the validity of the study.

A. BACKGROUND INFORMATION

Thifensulfuron-methyl is a sulfonylurea herbicide (Group 2) registered for post-emergence application to barley, canola, cotton, flax, field corn, oat, soybean and wheat for selective control of broadleaf weeds. It is absorbed through the foliage of treated weeds, inhibiting growth, causing necrosis of the growing plant, and eventual plant death. Permanent tolerances are established for thifensulfuron methyl in/on barley, canola, corn, cotton, flax, oat, rice, sorghum, soybean and wheat commodities, at levels ranging from 0.02 to 2.5 ppm (40CFR §180.439[a]).

For the current petition (9F7523), IR-4 is proposing a new use for thifensulfuron methyl on safflower. The chemical structure and nomenclature of thifensulfuron methyl are presented in Table A.1, below. The physicochemical properties of the technical grade of thifensulfuron methyl are presented in Table A.2, below.

TABLE A.1 Thifensulfuron Methyl Nomenclature.

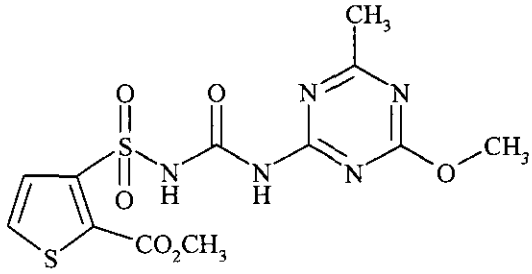
Chemical structure	
Common name	Thifensulfuron methyl
Molecular formula	$C_{12}H_{13}N_5O_6S_2$
Molecular weight	387.38
Company experimental name	DPX-M6316
IUPAC name	Methyl 3-(4-methoxy-6-methyl-I,3,5-triazin-2-ylcarbamoylsulfamoyl) thiophene-2-carboxylate
CAS name	Methyl 3-[[[[(4-methoxy-6-methyl-1,3,5- triazin-2-yl)amino]carbonyl]amino] sulfonyl]-2-thiophenecarboxylate
CAS registry number	79277-27-3
End-use product (EP)	Field trials: 75% ai DF, DuPont™ Harmony® GT XP, EPA Registration #352-446 Proposed use: 50% ai SG, DuPont™ Harmony® SG, EPA Registration #352-633

TABLE A.2 Physicochemical Properties of Thifensulfuron Methyl.

Parameter	Value	Reference
Melting point/range (°C)	171.1 ± 1.2	MRID #47138301 (D342084; D. Dotson; 17 April 2008)
pH	4.0	
Density (g/cm^3)	1.58 ± 0.004	
Water solubility (g/L at 25°C)	pH 5 0.223 pH 7 2.24 pH 9 8.83	
Solvent solubility (g/L at 25°C)	Acetone - 11.9 Acetonitrile - 7.3 Dichloromethane - 27.5 Ethanol - 0.9 Ethyl acetate - 2.6 Hexane - <0.1 Methanol - 2.6 Xylene - 0.2	
Vapor pressure (25°C)	1.7 x 10^{-8} Pa (1.3 x 10^{-10} mm Hg)	
Dissociation constant (pK_a)	4.0	

21

TABLE A.2 Physicochemical Properties of Thifensulfuron Methyl.			
Parameter	Value		Reference
Octanol/water partition coefficient (Log [K_{OW}])	pH 5 pH 7 pH 9	1.06 0.0222 0.0078	
UV/visible absorption (max, λ)	pH <2 pH 7 pH >10	224, 250 nm 233 nm 234 nm	

B. EXPERIMENTAL DESIGN

B.1. Application and Crop Information

A single safflower processing study was conducted in 2000 in ND. The 75% ai DF formulation of thifensulfuron methyl was applied to safflower, as a single broadcast foliar application 81 days before harvest, at the rate of 0.0186 lb ai/A (1X the field trial application rate). The application was made using ground equipment, in a spray volume of 15 GPA, and included the use of an NIS. The study use pattern is detailed in Table B.1.1, below.

Temperature recordings, and rainfall averages were reported to be within average historical values for the processing study period. Irrigation was not used at this trial site. The trial was conducted according to normal agricultural practices, and information was provided on maintenance pesticides, and fertilizers. Phytotoxic effects were noted at the field trial. Plants were reported to be a lighter green compared to plants in the untreated plots, but after 10 days the proper color returned, and the treated plots showed no other visible injury symptoms.

TABLE B.1.1 Study Use Pattern.							
Location (City, State; Year) [Trial ID]	EP[1]	Application					Adjuvants
		Method; Timing	Volume (GPA)	Rate (lb ai/A)	RTI[2] (Days)	Total Rate (lb ai/A)	
Williston, ND; 2000 [ND12]	75% ai DF	One broadcast foliar application; late vegetative to early bud.	15	0.0186	--	0.0186	NIS

1. EP = End-use Product (75% ai DF = Harmony® GT XP herbicide, EPA Registration #352-446).
2. RTI = Re-Treatment Interval (not relevant to this study, as only one treatment was applied to safflower).

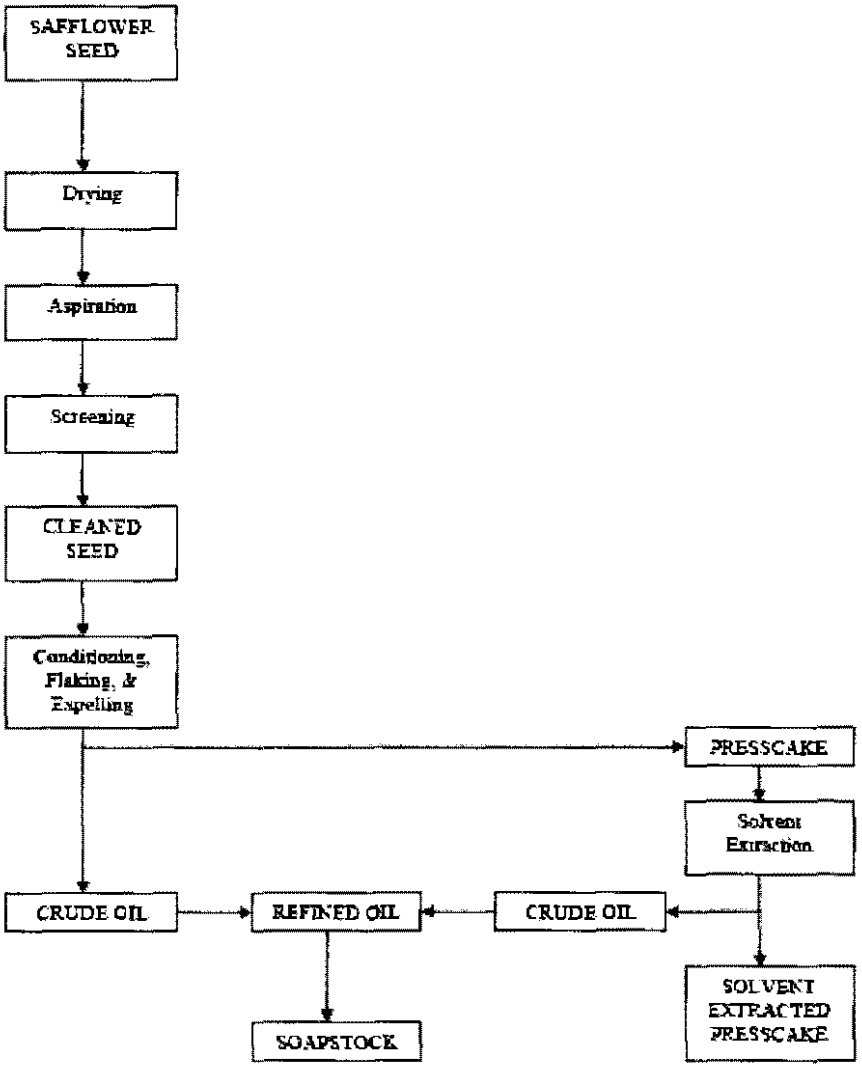
B.2. Sample Handling and Processing Procedures

Control and treated samples of safflower seeds for processing were harvested from the middle of each plot, and placed in the freezer at the field facility within an hour of collection. Seed samples intended for processing were shipped frozen (via ACDS freezer truck) to Texas A&M University, Food Protein Research and Development Center (in Bryan, TX).

Upon receipt at the processing facility, samples were stored frozen until processing. Samples were processed into safflower meal and refined oil within 57-66 days of harvest, using simulated commercial practices. Samples of seeds were dried in an oven (54-71°C) to adjust the percent moisture to 6-8% (on a wet weight basis) before processing. The petitioner submitted adequate descriptions of the processing procedures including material balance summaries. A flowchart of the processing procedure, copied without alteration from MRID #47641801, is presented in Figure 1, below. After processing, all samples were stored frozen until shipment (via ACDS freezer truck) to the analytical facility (North Dakota IR-4 Satellite Laboratory; Fargo, ND) for analysis. At the laboratory, a subsample of safflower seeds was ground and stored frozen (-24 to -14°C) until extraction and analysis.

FIGURE 1. Processing Flowchart for Safflower Seeds.

Figure 1 – Processing Flowchart for Safflower Seed



B.3. Analytical Methodology

Samples were analyzed for residues of thifensulfuron methyl using an HPLC photo-conductivity detection method (DuPont Method AMR-973-87), entitled *A Method for Analysis of*

the Herbicide, DPX-M6316 in Soybeans by Liquid Chromatography. A description of the method was included in the safflower processed food and feed submission.

For this method, residues were extracted from safflower seeds and meal by soaking the ground sample in 0.05 M sodium bicarbonate for a minimum of 2 hours, then adjusting the pH to 3.5 prior to homogenization in dichloromethane (DCM). The organic solvent was isolated, and extracted three times with 0.05 M $NaHCO_3$. The resulting aqueous extracts were combined, rinsed with hexane, and adjusted to pH 3.0-3.5 with HCl. The acidic solution was cleaned up on a C_{18} solid phase extraction (SPE) cartridge; residues were eluted with methanol/0.1% acetic acid in water (3:2, v:v). The analyte was then partitioned into DCM, evaporated to dryness, and reconstituted with DCM prior to loading onto a CN SPE cartridge. The analyte was eluted with 10% ethyl acetate in DCM (v:v). The eluate was evaporated to dryness, and reconstituted in n-hexane/isopropyl alcohol (3:1, v:v) prior to analysis by HPLC with photo-conductivity detection.

For safflower oil, the same method was used with several modifications. Since both oil and the analyte are very soluble in DCM, soaking in sodium bicarbonate was not required. As a result, the extraction and isolation procedure for oil was simplified by initiating the isolation with the back-extraction from DCM to 0.05 M $NaHCO_3$, and following the same procedure from that point.

The LLMV in each matrix was 0.050 ppm. The calculated LOQs were 0.027 ppm in safflower seeds, 0.039 ppm in meal, and 0.0068 ppm in oil, while the LODs were 0.009 ppm in seeds, 0.013 ppm in meal, and 0.0023 ppm in oil. The method was adequately validated prior to, and in conjunction with, the analysis of the field trial samples.

To support sample storage conditions and durations, a concurrent storage stability study was conducted. Three samples each of untreated safflower seeds, meal and refined oil were fortified with thifensulfuron methyl at 0.10 ppm, and then stored frozen for 631, 584 and 588 days, respectively.

C. RESULTS AND DISCUSSION

Sample storage conditions and durations for safflower seeds, meal and oil are summarized in Table C.2.1, below. Samples of safflower seeds were frozen for up to 608 days, and processed samples of meal and oil were stored frozen for up to 567 and 561 days, respectively, prior to analysis. The results of the concurrent storage stability study are presented in Table C.2.2, below. These data demonstrate that residues of thifensulfuron methyl are stable in fortified samples stored frozen for intervals of up to 631 days in safflower seeds, 584 days in meal, and 588 days in oil. The average corrected recovery was 92% from safflower seeds, 97% from safflower meal, and 108% from safflower oil. Zero-day data were not provided; IR-4 is reminded that storage stability studies should always include a zero-day sampling interval to establish the residue levels present at the time samples are placed into storage (see *OPPTS Residue Chemistry Test Guideline 860.1380[d][6][i]*). The concurrent storage stability data are

adequate to support the storage durations and conditions of samples from the safflower processing study.

Method validation and concurrent method recovery data are present in Table C.1, below. The HPLC photo-conductivity detection method (Method AMR-973-87) used for determining residues of thifensulfuron methyl in safflower seeds, meal and oil was adequately validated prior to, and in conjunction with, the analysis of the processing trial samples. Samples of safflower seeds, meal and oil were fortified with thifensulfuron methyl at 0.050-0.50 ppm for method validation, and 0.050-0.10 ppm for concurrent analysis. The concurrent recovery fortification levels adequately bracketed field trial residue results. Recoveries were within the generally recognized acceptable range of 70-120% from all samples. The method validation recovery was 84% with a standard deviation of 6% from safflower seeds, 82% with a standard deviation of 7% from safflower meal, and 91% with a standard deviation of 7% from safflower oil. The concurrent recovery averaged 81% with a standard deviation of 6% from seeds, averaged 73% from meal, and averaged 88% from oil. Adequate sample chromatograms and example calculations were provided. Apparent residues of thifensulfuron methyl were below the LLMV (<0.050 ppm) in one sample each of untreated safflower seeds, meal and oil.

Residue data from the safflower processing study are reported in Table C.3, below. Residues of thifensulfuron methyl were below the LLMV (<0.050 ppm) in safflower seed RAC samples harvested 81 days after treatment at the rate of 0.0186 lb ai/A (1X the field trial application rate). Following processing, residues of thifensulfuron methyl were <0.050 ppm in safflower meal and refined oil processed from treated safflower seeds. Processing factors could not be calculated because residues were below the LLMV in both the RAC and the processed fractions.

The theoretical processing factors for safflower meal and oil are 9.1X and 3.3X, respectively (*OPPTS Residue Chemistry Test Guideline 860.1520*, Table 3).

TABLE C.1 Summary of Method Validation and Concurrent Recoveries of Thifensulfuron Methyl from Safflower Commodities.

Matrix	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev.[1] (%)
Method Validation				
Safflower seeds[2]	0.05	6	82, 79, 81, 94, 90, 89	86 ± 6
	0.50	3	76, 79, 85	80 ± 5
	Total	**9**	**76-94**	**84 ± 6**
Safflower meal	0.05	3	70, 79, 83	77 ± 7
	0.50	3	91, 87, 79	86 ± 6
	Total	**6**	**70-91**	**82 ± 7**
Safflower oil	0.05	3	95, 93, 94	94 ± 1
	0.50	3	91, 77, 93	87 ± 9
	Total	**6**	**77-95**	**91 ± 7**

TABLE C.1 Summary of Method Validation and Concurrent Recoveries of Thifensulfuron Methyl from Safflower Commodities.

Matrix	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean ± Std. Dev. [1] (%)
Concurrent Recovery				
Safflower seeds [2]	0.05	4	71, 84, 83, 87	81 ± 7
	0.10	1	81 [3]	81
	Total	**5**	**71-87**	**81 ± 6**
Safflower meal	0.05	1	75	**73**
	0.10	1	70 [3]	
	Total	**2**	**70-75**	
Safflower oil	0.05	1	94	**88**
	0.10	1	82 [3]	
	Total	**2**	**82-94**	

1. Standard deviation is only calculated for sample sizes ≥3.
2. Recoveries from safflower seeds are also presented in the OPPTS 860.1500 DER for MRID #47641801.
3. Storage stability concurrent recovery (refer to Table C.2.2, below).

TABLE C.2.1 Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration [1] (Days)	Interval of Demonstrated Storage Stability [2] (Days)
Safflower seeds	-26 to -14	608	631
Safflower meal		567	584
Safflower oil		561	588

1. Interval from harvest to analysis. Extracts were stored 1-6 days prior to analysis.
2. Refer to Table C.2.2, below.

TABLE C.2.2 Stability of Thifensulfuron Methyl Residues in Safflower Seeds and Processed Commodities.

Commodity	Spike Level (ppm)	Storage Interval (Days)	Freshly Fortified Recovery (%)	Recoveries (%)	Corrected Recovery [1] (%)
Safflower seeds	0.10	631	81	70, 73, 80	86, 90, 99 (92)
Safflower meal	0.10	584 [2]	70	66, 68, 70	94, 97, 100 (97)
Safflower oil	0.10	588	82	68, 86, 112	83, 105, 137 (108)

1. Corrected for concurrent method recovery, with average corrected recovery reported in parentheses.
2. Note that the extract for safflower meal was stored frozen for 23 days prior to analysis.

24

TABLE C.3 Residue Data from Safflower Processing Study with Thifensulfuron Methyl[1]					
RAC	Processed Commodity	Total Rate (lb ai/A)	PHI (Days)	Total Residues (ppm)	Processing Factor
Safflower seeds	Seeds (RAC)	0.0186	81	<0.05, <0.05	--
	Meal			<0.05, <0.05	NC
	Oil			<0.05, <0.05	NC

1. The LLMV for thifensulfuron methyl residues in safflower seeds, meal and oil is 0.050 ppm.
2. NC = Not Calculated. The processing factor could not be calculated because residues were below the LLMV in both the RAC and the processed fractions.

D. CONCLUSION

Processing factors for thifensulfuron methyl in safflower seeds could not be calculated because residues were below the method LLMV (<0.050 ppm) in both the RAC and the processed commodities, meal and refined oil. An acceptable method was used for the quantitation of residues in safflower matrices, and adequate storage stability data are available to support sample storage conditions and durations.

E. REFERENCES

Ingredient: Thifensulfuron Methyl. Title: Label Amendments and Petition for Tolerances on Wheat Forage and Hay, Oat Forage and Hay, and Barley Hay. Summary of Analytical Chemistry and Residue Data.; D342084; D. Dotson; 17 April 2008.

F. DOCUMENT TRACKING

RDI: William T. Drew (30 September 2009); Dennis McNeilly (6 October 2009)
Petition Number: 9F7523
DP Number: 361945
PC Code: 128845

13544

R180720

Chemical Name: Thifensulfuron

PC Code: 128845
HED File Code: 11000 Chemistry Reviews
Memo Date: 1/19/2010
File ID: 00000000
Accession #: 000-00-0134

HED Records Reference Center
2/5/2010